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<i>2/52</i> <i>Fig.1(i)</i>	<i>3/52</i> <i>Fig.1(ii)</i>
<i>4/52</i> <i>Fig.1(iii)</i>	<i>5/52</i> <i>Fig.1(iv)</i>

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1	TCGGCCTCC GAAACC ATG AAC TTT CTG	
	Met Asn Phe Leu	
	1	
50	CTT GCC TTG CTG CTC TAC CTC CAC	
	Leu Ala Leu Leu Leu Tyr Leu His	
	15	
98	CCC ATG GCA GAA GGA GGA GGG CAG	
	Pro Met Ala Glu Gly Gly Gly Gln	
	30 35	
146	ATG GAT GTC TAT CAG CGC AGC TAC	
	Met Asp Val Tyr Gln Arg Ser Tyr	
	45 50	
194	GAC ATC TTC CAG GAG TAC CCT GAT	
	Asp Ile Phe Gln Glu Tyr Pro Asp	
	60 65	
242	TCC TGT GTG CCC CTG ATG CGA TGC	
	Ser Cys Val Pro Leu Met Arg Cys	
	80	
290	CTC GAG TGT GTG CCC ACT GAG GAG	
	Leu Glu Cys Val Pro Thr Glu Glu	
	95	
338	CGG ATC AAA CCT CAC CAA GGC CAG	
	Arg Ily Lys Pro His Gln Gly Gln	
	110 115	

Fig.1(i)

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CTG TCT TGG GTG CAT TGG AGC	49
Leu Ser Trp Val His Trp Ser	
5 10	
CAT GCC AAG TGG TCC CAG GCT GCA	97
His Ala Lys Trp Ser Gln Ala Ala	
20 25	
AAT CAT CAC GAA GTG GTG AAG TTC	145
Asn His His Glu Val Val Lys Phe	
40	
TGC CAT CCA ATC GAG ACC CTG GTG	193
Cys His Pro Ile Glu Thr Leu Val	
55	
GAG ATC GAG TAC ATC TTC AAG CCA	241
Glu Ile Glu Tyr Ile Phe Lys Pro	
70 75	
GGG GGC TGC TGC AAT GAC GAG GGC	289
Gly Gly Cys Cys Asn Asp Glu Gly	
85 90	
TCC AAC ATC ACC ATG CAG ATT ATG	337
Ser Asn Ile Thr Met Gln Ile Met	
100 105	
CAC ATA GGA GAG ATG AGC TTC CTA	385
His Ile Gly Glu Met Ser Phe Leu	
120	

Fig.1(ii)

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386	CAG CAC AAC AAA TGT GAA TGC AGA	
	Gln His Asn Lys Cys Glu Cys Arg	
	125	130
434	GAA AAT CCC TGT GGG CCT TGC TCA	
	Glu Asn Pro Cys Gly Pro Cys Ser	
	140	145
482	CAA GAT CCG CAG ACG TGT AAA TGT	
	Gln Asp Pro Gln Thr Cys Lys Cys	
		160
530	TGC AAG GCG AGG CAG CTT GAG TTA	
	Cys Lys Ala Arg Gln Leu Glu Leu	
		175
578	AAG CCG AGG CGG TGAGCCGGGC AGGAG	
	Lys Pro Arg Arg	
		190
630	GAACCAGATC TCTCACCAGG	

Fig.1(iii)

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CCA AAG AAA GAT AGA GCA AGA CAA	433
Pro Lys Lys Asp Arg Ala Arg Gln	
135	
GAG CGG AGA AAG CAT TTG TTT GTA	481
Glu Arg Arg Lys His Leu Phe Val	
150 155	
TCC TGC AAA AAC ACA GAC TCG CGT	529
Ser Cys Lys Asn Thr Asp Ser Arg	
165 170	
AAC GAA CGT ACT TGC AGA TGT GAC	577
Asn Glu Arg Thr Cys Arg Cys Asp	
180 185	
GAAGG AGCCTCCCTC AGCGTTTCGG	629
	649

Fig.1(iv)

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7/52 Fig.2(i)	8/52 Fig.2(ii)
9/52 Fig 2(iii)	10/52 Fig 2(iv)
11/52 Fig 2(v)	12/52 Fig 2(vi)

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1	CC ATG AGC CCT CTG CTC CGC CGC
	Met Ser Pro Leu Leu Arg Arg
	1 5
48	CTG GCC CCC GCC CAG GCC CCT GTC
	Leu Ala Pro Ala Gln Ala Pro Val
	20
96	CAG AGG AAA GTG GTG TCA TGG ATA
	Gln Arg Lys Val Val Ser Trp Ile
	35
144	CAG CCC CGG GAG GTG GTG GTG CCC
	Gln Pro Arg Glu Val Val Val Pro
	50 55
192	GTG GCC AAA CAG CTG GTG CCC AGC
	Val Ala Lys Gln Leu Val Pro Ser
	65 70
240	GGC TGC TGC CCT GAC GAT GGC CTG
	Gly Cys Cys Pro Asp Asp Gly Leu
	80 85
288	CAA GTC CGG ATG CAG ATC CTC ATG
	Gln Val Arg Met Gln Ile Leu Met
	100
336	GGG GAG ATG TCC CTG GAA GAA CAC
	Gly Glu Met Ser Leu Glu Glu His
	115

Fig.2(i)

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CTG CTG CTC GCC GCA CTC CTG CAG	47
Leu Leu Leu Ala Ala Leu Leu Gln	
10 15	
TCC CAG CCT GAT GCC CCT GGC CAC	95
Ser Gln Pro Asp Ala Pro Gly His	
25 30	
GAT GTG TAT ACT CGC GCT ACC TGC	143
Asp Val Tyr Thr Arg Ala Thr Cys	
40 45	
TTG ACT GTG GAG CTC ATG GGC ACC	191
Leu Thr Val Glu Leu Met Gly Thr	
60	
TGC GTG ACT GTG CAG CGC TGT GGT	239
Cys Val Thr Val Gln Arg Cys Gly	
75	
GAG TGT GTG CCC ACT GGG CAG CAC	287
Glu Cys Val Pro Thr Gly Gln His	
90 95	
ATC CGG TAC CCG AGC AGT CAG CTG	335
Ile Arg Tyr Pro Ser Ser Gln Leu	
105 110	
AGC CAG TGT GAA TGC AGA CCT AAA	383
Ser Gln Cys Glu Cys Arg Pro Lys	
120 125	

Fig. 2(ii)

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384	AAA	AAG	GAC	AGT	GCT	GTG	AAG	CCA
	Lys	Lys	Asp	Ser	Ala	Val	Lys	Pro
			130					135
432	CGT	CCC	CAG	CCC	CGT	TCT	GTT	CCG
	Arg	Pro	Gln	Pro	Arg	Ser	Val	Pro
			145					150
480	CCC	TCC	CCA	GCT	GAC	ATC	ACC	CAT
	Pro	Ser	Pro	Ala	Asp	Ile	Thr	His
			160					165
528	GCC	CAC	GCT	GCA	CCC	AGC	ACC	ACC
	Ala	His	Ala	Ala	Pro	Ser	Thr	Thr
					180			
576	GCT	GCC	GCT	GCC	GAC	GCC	GCA	GCT
	Ala	Ala	Ala	Ala	Asp	Ala	Ala	Ala
					195			

Fig. 2(iii)

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GAC	AGG	GCT	GCC	ACT	CCC	CAC	CAC	431
Asp	Arg	Ala	Ala	Thr	Pro	His	His	
				140				
GGC	TGG	GAC	TCT	GCC	CCC	GGA	GCA	479
Gly	Trp	Asp	Ser	Ala	Pro	Gly	Ala	
				155				
CCC	ACT	CCA	GCC	CCA	GGC	CCC	TCT	527
Pro	Thr	Pro	Ala	Pro	Gly	Pro	Ser	
		170					175	
AGC	GCC	CTG	ACC	CCC	GGA	CCT	GCC	575
Ser	Ala	Leu	Thr	Pro	Gly	Pro	Ala	
	185						190	
TCC	TCC	GTT	GCC	AAG	GGC	GGG	GCT	T 624
Ser	Ser	Val	Ala	Lys	Gly	Gly	Ala	
200					205			

Fig.2(iv)

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625 AGAGCTCAAC CCAGACACCT GCAGGTGCCG
685 GACTCAGCAG GGTGACTTGC CTCAGAGGCT
745 GGTAAAAAAC AGCCAAGCCC CCAAGACCTC
805 GCCTCTCAGA GGGCTCTTCT GCCATCCCTT
865 GAGTTGGAAG AGGAGACTGG GAGGCAGCAA
825 GGAGTACTGT CTCAGTTTCT AACCACTCTG
985 CTCCCCTCAC TAAGAAGACC CAAACCTCTG
1045 CTGTGACCCC CAACCCTGAT AAAAGAGATG

Fig.2(v)

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GAAGCTGCGA AGGTGACACA TGGCTTTTCA	684
ATATCCCAGT GGGGGAACAA AGGGGAGCCT	744
AGCCCAGGCA GAAGCTGCTC TAGGACCTGG	804
GTCTCCCTGA GGCCATCATC AACAGGACA	864
GAGGGGTCAC ATACCAGCTC AGGGGAGAAT	924
TGCAAGTAAG CATCTTACAA CTGGCTCTTC	984
CATAATGGGA TTTGGGCTTT GGTACAAGAA	1044
GAAGGAAAAA AAAAAAAAAA	1094

Fig.2(vi)

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Fig. 3(i)	Fig. 3(ii)

Variable	Mean	SD	Min	Max
Age	34.5	10.2	22	55
Gender	Male	Female		
Marital Status	Married	Single		
Education	High School	College		
Occupation	Manager	Worker		
Income	\$25,000	\$35,000		
Health Status	Good	Fair		
Exercise Frequency	Weekly	Monthly		
Stress Level	Low	High		
Sleep Quality	Good	Poor		
Dietary Habits	Healthy	Unhealthy		
Alcohol Consumption	Occasional	Frequent		
Tobacco Use	Non-user	User		
Family Size	2	3		
Home Ownership	Owner	Renter		
Commute Time	15 min	30 min		
Work Hours	40 hrs/week	50 hrs/week		
Job Satisfaction	High	Low		
Life Satisfaction	High	Low		
Overall Well-being	Good	Fair		

SCORE = 181 (92.4 BITS), EXPECT = 6.4e-20,
IDENTITIES = 33/75 (44%), POSITIVES = 48/75

QUERY: 91 PTGQHQVRMQILMIR 105
PT + + MQI+ I+
SBJCT: 96 PTEESNITMQIMRIK 110

```

QUERY:      110  QLGEMSLEEHSQCECRPKK  128
              ++GEMS  +H+  CECRPKK
SBJCT:      116  HIGEMSFLQH NKCECRPKK  134

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```

QUERY:      202 RCQGRGLELNPDTCRCRKLRR 222
              RC +R LELN  TCRC K  RR
SBJCT:      195 RCKARQLELNERTCRCDKPRR 215

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QUERY:      187  DPRTCRCRCR  196
              DP+TC+C  C+
SBJCT:      181  DPQTCKCSCK  190

```

Fig.3(i)

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GROWTH FACTOR PRECURSOR (VEGF)

 $P = 6.4e-20$
(64%)

MGTVAKQLVPSCVTVQRCGGCCPDDGLECV 90
+ PSCV + RCGGCC D+GLECV
PDEIEYIFKPSCVPLMRCGGCCNDEGLECV 95

 $\text{POISSON } P(2) = 9.1e-12$
(84%) $\text{POISSON } P(3) = 3.6e-18$
(71%) $\text{POISSON } P(4) = 7.3e-10$
(90%)*Fig. 3(i)*

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17/52 <i>Fig.4(i)</i>	18/52 <i>Fig 4(ii)</i>
19/52 <i>Fig.4(iii)</i>	20/52 <i>Fig.4(iv)</i>

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Gap Weight:3.00 Average Match:1.000
 Length Weight:0.100 Average Mismatch:-0.900
 Quality:100.9 Length:739
 Ratio:0.175 Gaps:30
 Percent Percent
 Similarity:69.703 Identity:69.703

```

28   ATGAGCCCTCTGCTCCGCCGCCTGC
      |||| | ||||| | ||
17   ATGAACTTTCTGCT.....GTCT..

68   TGCAGCTGGCCCCCGCCCAGGCCCC
      ||| ||| || | ||| |||
57   TGCTGCTCTACCTCCACCATGCCAA

118  CACCAGAGGA.....
      |||||
106  AGAAGGAGGAGGGCAGAATCATCAC

140  GTGTATACTCGC.GCTACCTGCCAG
      || ||| ||| |||| |||||
152  GTCTATCAGCGCAGCTA.CTGCCAT

194  T....GA.....CTGTGGAGCTCAT
      |   ||   ||| ||| ||
201  TCCAGGAGTACCCTGATGAGATCGA

235  CCCAGCTGCGTGACTGTGCAGCGCT
      ||   ||| ||| | || ||| |
239  CCATCCTGTGTGCCCTGATGCGAT

285  CCTGGAGTGTGTGCCCCACTGGGCAG
      ||||| ||||| ||||| ||| ||
289  CCTGGAGTGTGTGCCCCACTGAGGAG
  
```

Fig.4(i)

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TGCTCGCCGCACT.....CC	67
...TGGGTGCATTGGAGCCTTGCCT	56
TGTCTCCCAGCCTGATGCCCCTGGC	117
GTGGTCCCAGGCTGCA.CCCATGGC	105
.AAGTGGTG....TCATGGATAGAT	147
GAAGTGGTGAAGTTCATG....GAT	151
CCCCGGGAG...GTGGTGGTGCCCT	193
CCAATCGAGACCCTGGTGGACATCT	200
GGGCACCGTGGCCAAACAGCTGGTG	234
GTACATCTT...CAA.....G	238
GTGGTGGCTGCTGCCCTGACGATGG	284
GCGGGGGCTGCTGCAATGACGAGGG	288
CACCAAGTCCGGATGCAGAT.....	329
TCCAACATCACCATGCAGATTATGC	338

Fig.4(ii)

SUBSTITUTE SHEET (RULE 26)

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```
330      .....CCTCATGATCCGGTACC
          |||||
339      GGATCAAACCTCA.....C

369      GTCCCTGGAAGAACACAGCCAGTGT
          | | | | | | | | | | | |
376      GAGCTTCCTACAGCACAACAAATGT

419      GTGCTGTGAAGCCAGACAGGGCTGC
          | | | | | | | |
423      G.....AGCAAGACAAG.....

469      CGTTCTGTTCCGGGCTGGGACTCTG
          | | | | | | | |
443      ...TGTGGGCCTTGCTCAGA.....

519      CATCACCCATCCCCTCCAGCCCCA

468      .....

569      GC.....ACCACCAGCGCCC
          || | | |
469      GCATTGTGTTGTACAA.....

609      TGCCGACGCCGCAGCTTCCTCCGTT
          || | | | | | | | |
509      TG.CAAAAACACAGACTC..GCGTT

657      AACCCAGACACCTGCAGGTGCCGGA
          || | |
554      AACGAACGTACTTGCAGATGTGACA
```

Fig.4(iii)

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CGAGCAGTCAGC...TGGGGGAGAT	368
CAAG..GCCAGCACATAGGAGAGAT	375
GAATGCAGACCTAAAAAAAGGACA	418
GAATGCAGACC...AAAGAAAGATA	422
CACTCCCCACCACCGTCCCCAGCCC	468
.....AAAATCCC.....	442
CCCCCGGAGCACCTCCCCAGCTGA	518
...GCGGAGAA.....	467
GGCCCCTCTGCCCACGCTGCACCCA	568
.....A	468
TGACCCCCGGACCTGCCGCTGCCGC	608
.GATCCGCAGACGTGTAAATGTTCC	508
GCCAAGGGCGGGGC..TTAGAGCTC	656
GC..AAGGCGAGGCAGCTTGAGTTA	553
AGCTGCGAAGGTGA	695
AGCCGAGGCGGTGA	592

Fig.4(iv)

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22/52 Fig 5(i)	23/52 Fig.5(ii)	24/52 Fig 5(iii)
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165SOMSQ.MSF.msf MSF:687

Type: D Tuesday, June 20, 1995

Check:3140

	1
VEGF165	ATGAACTTTCTGCTGTCTTGGGTG
SOM175	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e6	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e6&7	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e4	ATGAGCCCTCTGCTCCGCCGCCTG
	81
VEGF165	CACCCATGGCAGAAGGAGGAGGGC
SOM175	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e6	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e6&7	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e4	TGCCCCTGGCCACCAGAGGAAAGT
	161
VEGF165	CCAATCGAGACCCTGGTGGACATC
SOM175	GTGGTGGTGGCCCTTGACTG.TGGA
SOM175-e6	GTGGTGGTGGCCCTTGACTG.TGGA
SOM175-e6&7	GTGGTGGTGGCCCTTGACTG.TGGA
SOM175-e4	GTGGTGGTGGCCCTTGACTG.TGGA
	241
VEGF165	GATGCGATGCGGGGGCTGCTGCAA
SOM175	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e6	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e6&7	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e4	GCAGCGCTGTGGTGGCTGCTGCCC

Fig.5(i)

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CATTGGAGCCTTGCCTTGCTGCTCTACC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC

AGAATCATCACGAAGTGGTGAAGTTCAT
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC

TTCCAGGAGTACCCTGATGAGATCGAGT
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC

TGACGAGGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT

Fig.5(ii)

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80

TCCACCATGCCAAGTGGTCCCAGGCTG.
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA

160

GGATGTCTATCAGCGCAGCTACTGCCAT
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG

240

ACATCTTCAAGCCATCCTGTGTGCCCCT
TGGTGCCCAG.....CTGCGTGA CTGT
TGGTGCCCAG.....CTGCGTGA CTGT
TGGTGCCCAG.....CTGCGTGA CTGT
TGGTGCCCAG.....CTGCGTGA CTGT

320

GAGGAGTCCAACATCACCATGCAGATTA
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC

Fig.5(iii)

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VEGF165	TGCGGATCAAACCTCACCAAGGCC
SOM175	TCATGATCCGG...TACCCGAGCA
SOM175-e6	TCATGATCCGG...TACCCGAGCA
SOM175-e6&7	TCATGATCCGG...TACCCGAGCA
SOM175-e4

401

VEGF165	AAGAAAGATAG.....AGCAA
SOM175	AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e6	AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e6&7	AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e4	AAAAAGGACAGTGCTGTGAAGCCA

481

VEGF165AAGCA.....
SOM175	CTCTGCCCCCGGAGCACCCCTCCCC
SOM175-e6
SOM175-e6&7
SOM175-e4	CTCTGCCCCCGGAGCACCCCTCCCC

561

VEGF165	A.....GATCCGCA
SOM175	GCACCACCAGCGCCCTGACCCCCG
SOM175-E6	GCACCACCAGCGCCCTGACCCCCG
SOM175-e6&7
SOM175-e4	GCACCACCAGCGCCCTGACCCCCG

641

VEGF165	TTGAGTTAAACGAACGTACTTGCA
SOM175	TAGAGCTCAACCCAGACACCTGCA
SOM175-e6	TAGAGCTCAACCCAGACACCTGCA
SOM175-e6&7
SOM175-e4	TAGAGCTCAACCCAGACACCTGCA

Fig.5(iv)

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AGCACATAGGAGAGATGAGCTTCCTACA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
.....

GACAAGAA....AATCCCTGTGG.....
GACAGGGCTGCCACTCCCCACCACCGTC
GATAG.....
GATAG.....
GACAGGGCTGCCACTCCCCACCACCGTC

.....
AGCTGACATCACCCATCCCACTCCAGCC
.....CC
.....
AGCTGACATCACCCATCCCACTCCAGCC

GACGTGTAAATGTTCTTGCAAAAAC.AC
GACCTGCCGCTGCCGCTGCCGACGCCGC
GACCTGCCGCTGCCGCTGCCGACGCCGC
.....
GACCTGCCGCTGCCGCTGCCGACGCCGC

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GATGTGACAAGCCGAGGCGGTGA
GGTGCCGGAAGCTGCCGAAGGTGA
GGTGCCGGAAGCTGCCGAAGGTGA
.GTGCCGGAAGCTGCCGAAGGTGA
GGTGCCGGAAGCTGCCGAAGGTGA

Fig.5(v)

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400
GCACAACAAATGTGAATGCAGACC...A
ACACAGCCAGTGTGAATGCAGACCTAAA
ACACAGCCAGTGTGAATGCAGACCTAAA
ACACAGCCAGTGTGAATGCAGACCTAAA
.....CCTAAA

480
.....GCCTTGCTCAGAGCGGAGA
CCCAGCCCCGTTCTGTTCCGGGCTGGGA
.....
.....
CCCAGCCCCGTTCTGTTCCGGGCTGGGA

560
.....TTTGTT.....TGTAC..A
CCAGGCCCCCTCTGCCCACGCTGCACCCA
CCAGGCCCCCTCTGCCCACGCTGCACCCA
.....
CCAGGCCCCCTCTGCCCACGCTGCACCCA

640
AGACTCG..CGTTGCAAGGCGAGGCAGC
AGCTTCCTCCGTTGCCAAGGGCGGGGCT
AGCTTCCTCCGTTGCCAAGGGCGGGGCT
.....
AGCTTCCTCCGTTGCCAAGGGCGGGGCT

Fig.5(vi)

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<p><i>Fig 6(i)</i></p> <p>29/52</p>	<p><i>Fig 6(ii)</i></p> <p>30/52</p>
<p><i>Fig 6(iii)</i></p> <p>31/52</p>	

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VEGF ₁₆₅	M	N	F	L	L	S	W	V	H	W	S	L	A	L	L	L	Y	L	H	H	A	K	W	S	Q	A	A	P
SOM175 _{Short}	M	S	P	L	L	R	R	L	L	.	.	L	A	A	L	L	Q	L	A	P	A	Q	A	P
VEGF ₁₆₅	I	F	Q	E	Y	P	D	E	I	E	Y	I	F	K	P	S	C	V	P	L	M	R	C	G	G	C	C	N
SOM175 _{Short}	L	T	V	E	L	M	G	T	V	A	K	Q	L	V	P	S	C	V	T	V	Q	R	C	G	G	C	C	P
VEGF ₁₆₅	F	L	Q	H	N	K	C	E	C	R	P	K	K	D	R	A
SOM175 _{Short}	L	E	E	H	S	Q	C	E	C	R	P	K	K	K	D	S	A	V	K	P	D	R	A	A	T	P	H	
VEGF ₁₆₅	C	K	S	C	K	N	T	D	S	R	C	K	A	R	Q	L	E	L	N	E	R	T	C	R	C	D	K	
SOM175 _{Short}	H	A	A	P	S	T	T	S	A	L	T	P	G	P	A	A	A	A	D	A	A	S	S	V	A	K	K	
OR...																												
VEGF ₁₆₅	M	N	F	L	L	S	W	V	H	W	S	L	A	L	L	L	Y	L	H	H	A	K	W	S	Q	A	A	P
SOM175 _{Long}	M	S	P	L	L	R	R	L	L	.	.	L	A	A	L	L	Q	L	A	P	A	Q	A	P
VEGF ₁₆₅	I	F	Q	E	Y	P	D	E	I	E	Y	I	F	K	P	S	C	V	P	L	M	R	C	G	G	C	C	N
SOM175 _{Long}	L	T	V	E	L	M	G	T	V	A	K	Q	L	V	P	S	C	V	T	V	Q	R	C	G	G	C	C	P
VEGF ₁₆₅	F	L	Q	H	N	K	C	E	C	R	P	K	K	D	R	A
SOM175 _{Long}	L	E	E	H	S	Q	C	E	C	R	P	K	K	K	D	S	A	V	K	P	D	R	A	A	T	P	H	
VEGF ₁₆₅	G	P	C	S	E	R	R	K	H	L	F	V	Q	D	P	Q	T	C	K	C	S	C	K	N	T	D	S	.
SOM175 _{Long}	P	R	C	T	Q	H	H	Q	R	.	.	P	D	P	R	T	C	R	C	R	C	R	R	R	R	S	F	L

Fig.6(i)

Fig.6(i)

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M A E G G G Q N	H H E .	V V K F M	D V Y Q	R S Y Q	R S Y Q	C H C	P I E	T L V	D	60
V S Q P D A P G H	Q R K	V V S W I	D V Y T	R A T	R A T	C C P	R E V	V V P	P	55
D E G L E C V P T	E E S N I	T M Q I	I M R I	I K P H Q	I K P H Q	G G Q H I	G E M S			121
D D G L E C V P T	G Q H Q V	R M Q I	I L M I	I R . Y P S S	I R . Y P S S	Q L G E M S				115
.	R Q E N	P C G P	C S E R R	K H L F .	K H L F .	V Q D P	Q T			170
R P Q P R S V P G W D S A	P G A P	S P A D I	T H	P T P A P G P	P T P A P G P	S A				175
P R R										
G G A										

191

207

M A E G G G Q N	H H E .	V V K F M	D V Y Q	R S Y Q	R S Y Q	C H C	P I E	T L V	D	60
V S Q P D A P G H	Q R K	V V S W I	D V Y T	R A T	R A T	C C P	R E V	V V P	P	55
D E G L E C V P T	E E S N I	T M Q I	I M R I	I K P H Q	I K P H Q	G G Q H I	G E M S			121
D D G L E C V P T	G Q H Q V	R M Q I	I L M I	I R . Y P S S	I R . Y P S S	Q L G E M S				115
R Q E N P	
R P Q P R S V P G W D S A	P G A P	S P A D I	T H	P T P A P G P	P T P A P G P	L C				170
R C K A R Q	L E L N	E R	T C R C	D K P R R	T C R C	D K P R R				191
R C Q G R	L E L N	P D	T C R C	R K L R R	T C R C	R K L R R				222

Fig. 6(ii)

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Areas of 100% homology are boxed and conserved residues thought to be involved in homodimerisation are underlined. The VEGF sequence depicted includes the 26 amino acid leader sequence (removal of which gives rise to mature VEGF₁₆₅) giving a total length of 191 amino acids.

Homology of SOM175 to VEGF₁₆₅ is 27% (33%) at the protein level, however within this are blocks of 100% homology. In particular, many structural residues are conserved including those thought to be involved in homodimerisation of VEGF (by comparison with PDGF).

ie. Cysteine-47

Proline-70, Cysteine-72, Valine-74

Arginine-77, Cystein-78, Glycine-80, Cysteines-81 & 82

Cysteine-89, Proline-91

Cysteines 122 & 124

Fig.6(iii)

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SPLICE VARIANTS OF SOM175

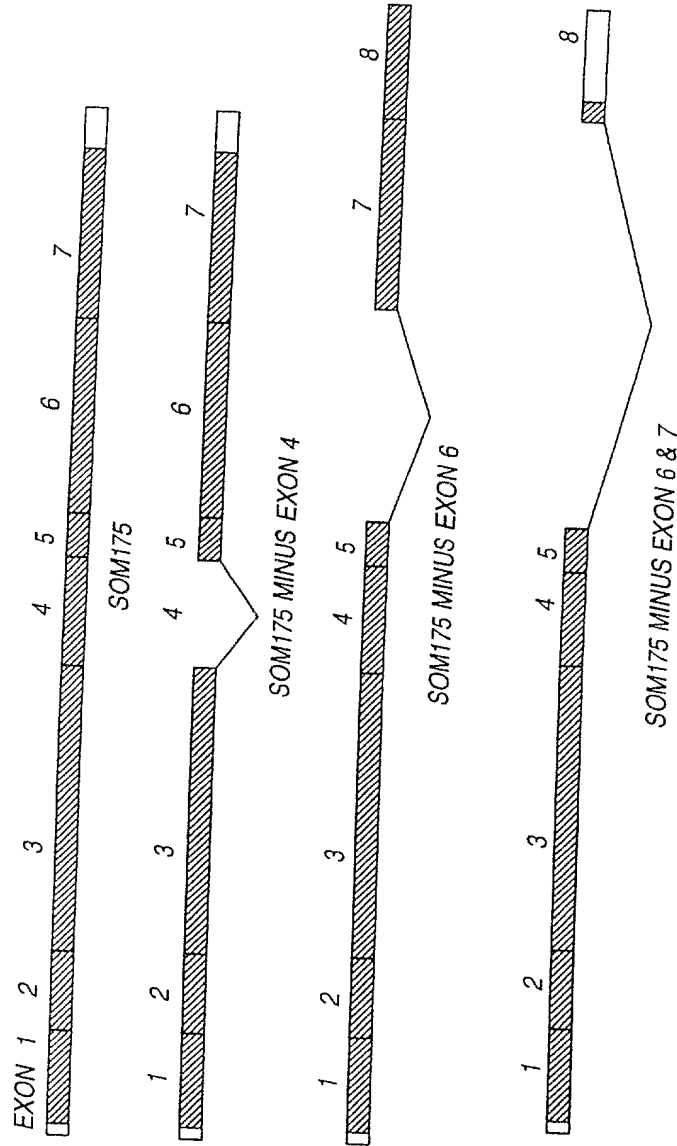


Fig.7

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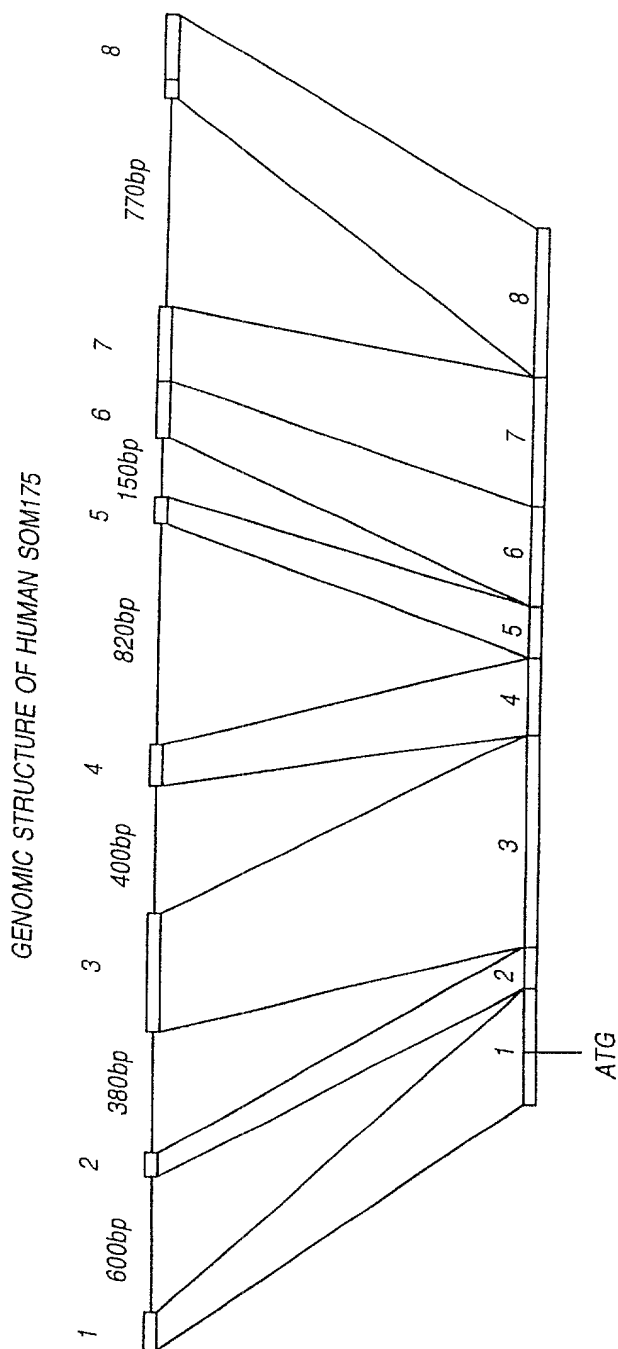


Fig.8A

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5'UTR... ATGAGG	*Exon 1 (60bp)	GGCCAG gtacgtgagg
tctcccacag GCCCCT	Exon 2 (43bp)	GGAAAG aatacttaca
tctgctccca TGGTGT	Exon 3 (187bp)	ATGCAG gtccgagatg
ctgaatacacag ATCCTC	Exon 4 (73bp)	ATGCAG gtgtcaggca
actttttcaag ACCTAA	Exon 5 (34bp)	AGACAG gtgagtcttt
ctcctccgta GGCTGC	Exon 6 (101bp)	CTCCAG cccaggccc
cccactccag CCCCAG	Exon 7 (109bp)	ACCCAG acacctgtag
ccctgctcag GTGCCG	*Exon 8 (22bp)	AGG TGA ...3'UTR

Fig.8B

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36/52 Fig 9(i)	37/52 Fig. 9(ii)
38/52 Fig. 9(iii)	39/52 Fig. 9(iv)

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-163 gcacgagctcagggccgctcgctgcggcgctg
-103 gggggccgcggaggagccgccccctgcgcc
-43 ggcggtctctggctgacccccccccacaccg

16 CGTCGCCTGCTGCTTGTTGCACTGCTGCAG
R R L L L V A L L Q

76 TTTGATGGCCCCAGTCACCAGAAGAAAGTG
F D G P S H Q K K V

136 ACATGCCAGCCCAGGGAGGTGGTGGTGCCT
T C Q P R E V V V P

196 AAACAAC TAGTGCCCAGCTGTGTGACTGTG
K Q L V P S C V T V

256 GGCCTGGAATGTGTGCCCAGTGGGCAACAC
G L E C V P T G Q H

316 TACCCGAGCAGTCAGCTGGGGGAGATGTCC
Y P S S Q L G E M S

376 CCTAAAAAAGGAGAGTGCTGTGAGGCCA
P K K K E S A V R P

436 CAGCCCCGCTCTGTTCCGGGCTGGGACTCT
Q P R S V P G W D S

Fig.9(i)

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cgttgcgctgcctgcgcccagggtcgga
 ccgccccgggtccccgggtccgcgccatgg
 ccgggctagggccccgATGAGCCCCCTGCTG
 M S P L L -17
 ↓
 CTGGCTCGCACCCAGGCCCTGTGTCCCAG
 L A R T Q A P V S Q 4

 GTGCCATGGATAGACGTTTATGCACGTGCC
 V P W I D V Y A R A 24

 CTGAGCATGGAACCTCATGGGCAATGTGGTC
 L S M E L M G N V V 44

 CAGCGCTGTGGTGGCTGCTGCCCTGACGAT
 Q R C G G C C P D D 64
 ↓
 CAAGTCCGAATGCAGATCCTCATGATCCAG
 Q V R M Q I L M I Q 84
 ↓
 CTGGGAGAACACAGCCAATGTGAATGCAGA
 L G E H S Q C E C R 104
 ↓
 GACAGGGTTGCCATACCCCACCACCGTCCC
 D R V A I P H H R P 124

ACCCCGGGAGCACCCCTCCCCAGCTGACATC
 T P G A P S P A D I 144

Fig.9(ii)

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496 ATCCATCCCACTCCAGCCCCAGGATCCTCT
 I H P T P A P G S S
 S P R I L

556 CTGACCCCCGGACCTGCCGTTGCCGCTGTA
 L T P G P A V A A V
 P D P R T C R C R C

616 GGGGCTTAGAGCTCAACCCAGACACCTGTA
 G A *
 R G L E L N P D T C

676 ctttccagactccacgggcccggctgcttt
736 agcacaggcgtaacctcctcagtcctgggag
796 gagctctctcgccatcttttatctcccaga
856 atgtctcacctcaggggccagggtactctc
916 ttctggctggctgtctcccctcactatgaa
976 gggttctgttatgataactgtgacacacac
1036 gacactaaaaaaaaaaaaaaaaaaaaaaaaa

Fig.9(iii)

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GCCCGCCTTGCACCCAGCGCCGCCAACGCC
 A R L A P S A A N A 164
 C P P C T Q R R Q R 130

 GACGCCGCGCTTCCTCCATTGCCAAGGGC
 D A A A S S I A K G 184
 R R R R F L H C Q G 150
 ↓
 GGTGCCGGAAGCCGCGAAAGTGAcaagctg
 186
 R C R K P R K * 167

 tatggccctgcttcacagggagaagagtgg
 gtcactgccccaggacctggaccttttaga
 gctgccatctaacaattgtcaaggaaacctc
 tcacttaaccaccctgggtcaagtgagcatc
 aaccccaaacttctaccaataacgggattt
 acacactcacactctgataaaagagatgga
 aaaaaaaaaa

Fig.9(iv)

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41/52	42/52
Fig 10(i)	Fig 10(ii)

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A

hVRF167	-21	MSPLLRRLLLLAALLQLAPAQAP	↓
mVRF167	-21	MSPLLRRLLLLVALLQLARTQAP	
hVRF167	30	EVVVPLTVELMGTVAKQLVPSC	
		:	
mVRF167	30	EVVVPLSMELMGNVVKQLVPSC	
hVRF167	80	ILMIRYPSSQLGEMSLEEHSQC	
		:	
mVRF167	80	ILMIQYPSSQLGEMSLGEHSQC	
hVRF167	130	RPDPRTCRCRCRRRSFLRCQGR	
		:	
mVRF167	130	RPDPRTCRCRCRRRFLHCQGR	

B

hVRF186	116	RAATPHHRPQPRSVPGWDSAPG
mVRF186	116	RVAIPHHRPQPRSVPGWDSTPG
hVRF186	166	TPGPAAAAADAAASSVAKGGA*
		:
mVRF186	166	TPGPAVAAVDAAASSIAKGGA*

Fig.10(i)

[illegible][illegible]

[illegible]

☐ ☐ ☐

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	5
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Fig. 10(ii)

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44/52	45/52
Fig 11(i)	Fig 11(ii)

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mVRF167	-21	MSPLLRRLLVALLQL..	: :
mVEGF188	-26	MNFLLSVHWTALLLYLHH	
mVRF167	25	TCQPREVVVPLSMELMGNVV	: : : :
mVEGF188	24	YCRPIETLVDIFQEYPDEIE	
mVRF167	75	QVRMQILMIQYPSSQ.LGEM	: : :
mVEGF188	74	NITMQIMRIKPHQSQHIGEM	
mVRF167	119ILCPPC	:
mVEGF188	124	QKRKRKKSFRKSWSVHCEPC	
mVRF167	152	GLELNPDTCRCKPRK	:
mVEGF188	173	QLELNERTCRCDKPRR	

Fig.11(i)

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AR.TQAPVSQFDGPSHQKKVVPWIDVYARA	24
: : : : : : :	
AKWSQAAPTT.EGEQKSHEVIKFMDVYQRS	23
KQLVPSCVTVQRCGGCCPDDGLECVPTGQH	74
: : : : : : :	
YIFKPSCVPLMRCAGCCNDEALECVPTSES	73
SLGEHSQCECRPKKKESAVRPDSPR.....	118
: :	
SFLQHSRCECRPKKDRTKPEKKSVRGKGKG	123
TQRRQR...PDPRTCRCRCRRRRFLHCQGR	151
: : : : : :	
SERRKHLFVQDPQTCKCCKNTDS.RCKAR	172
	167
	188

Fig.11(ii)

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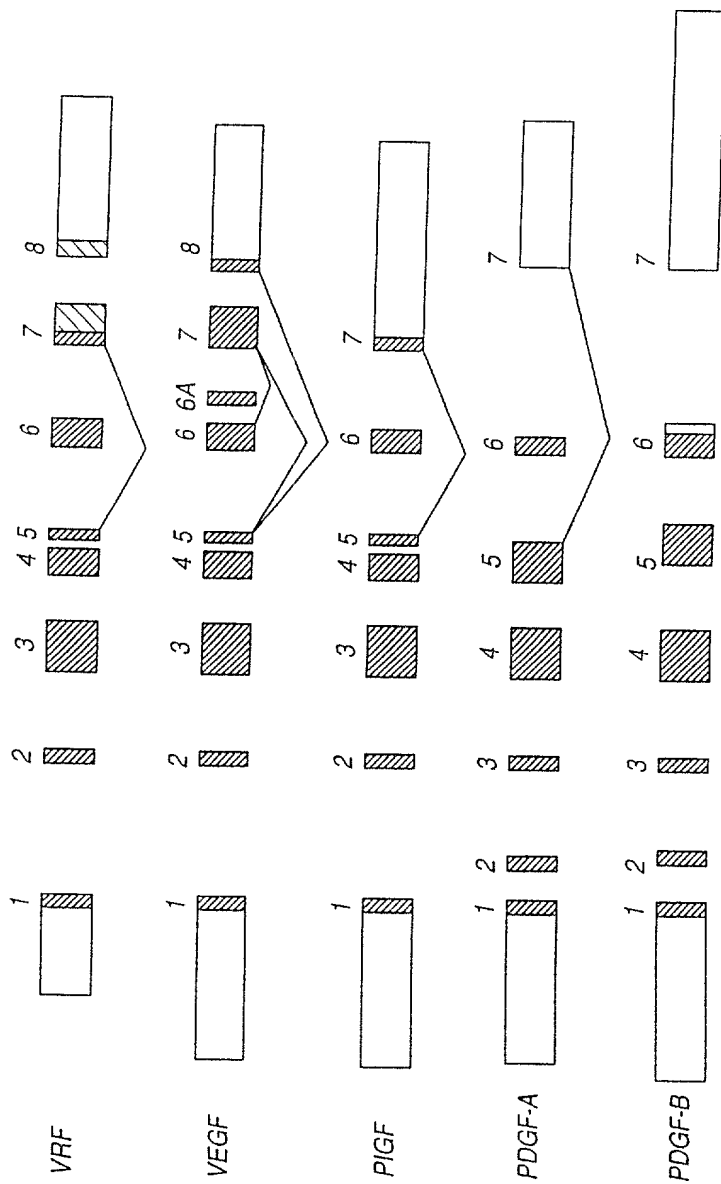


Fig.12

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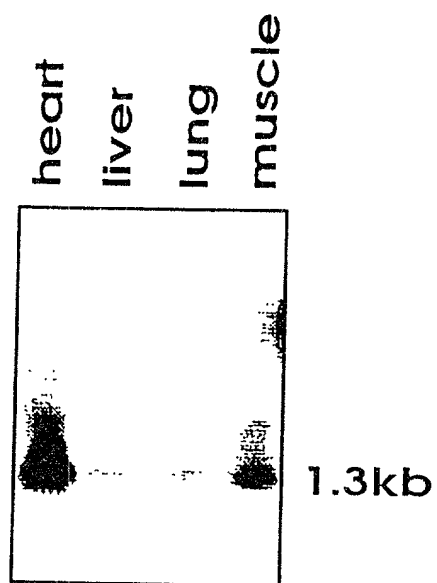


Fig.13

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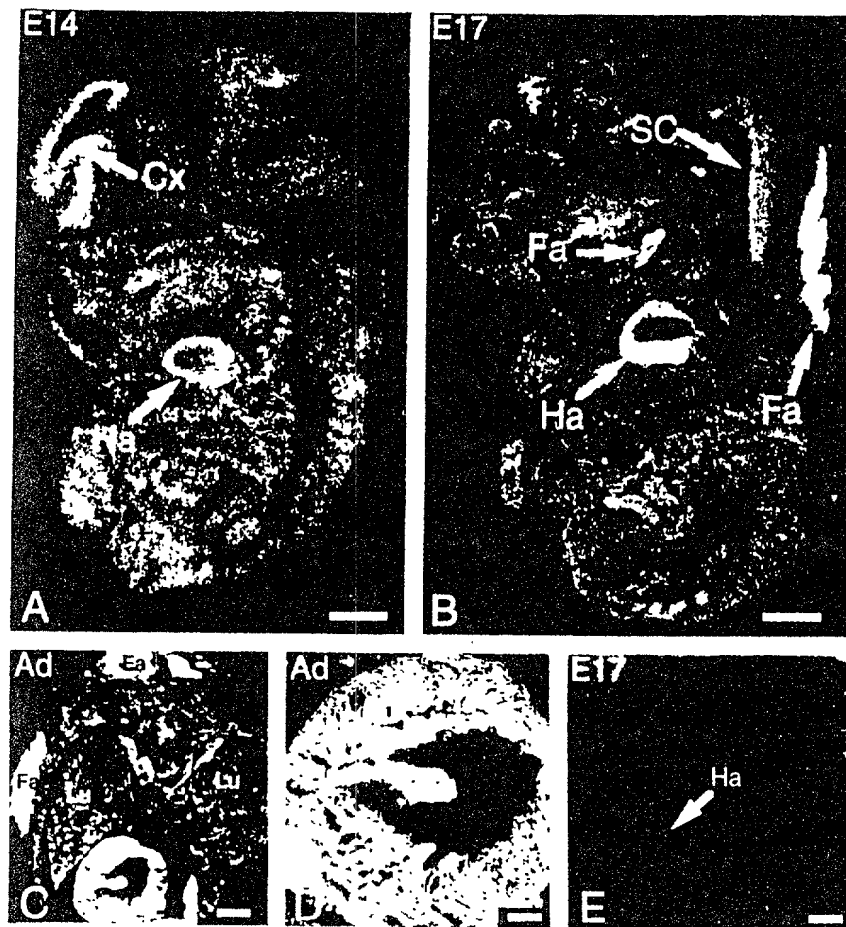


Fig.14

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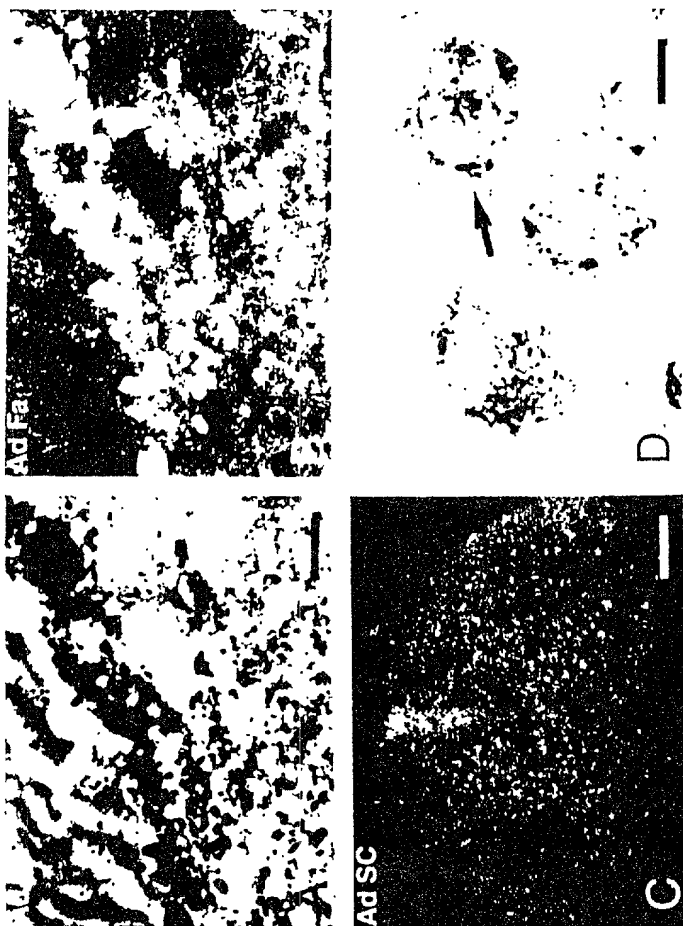


Fig.15

50/52

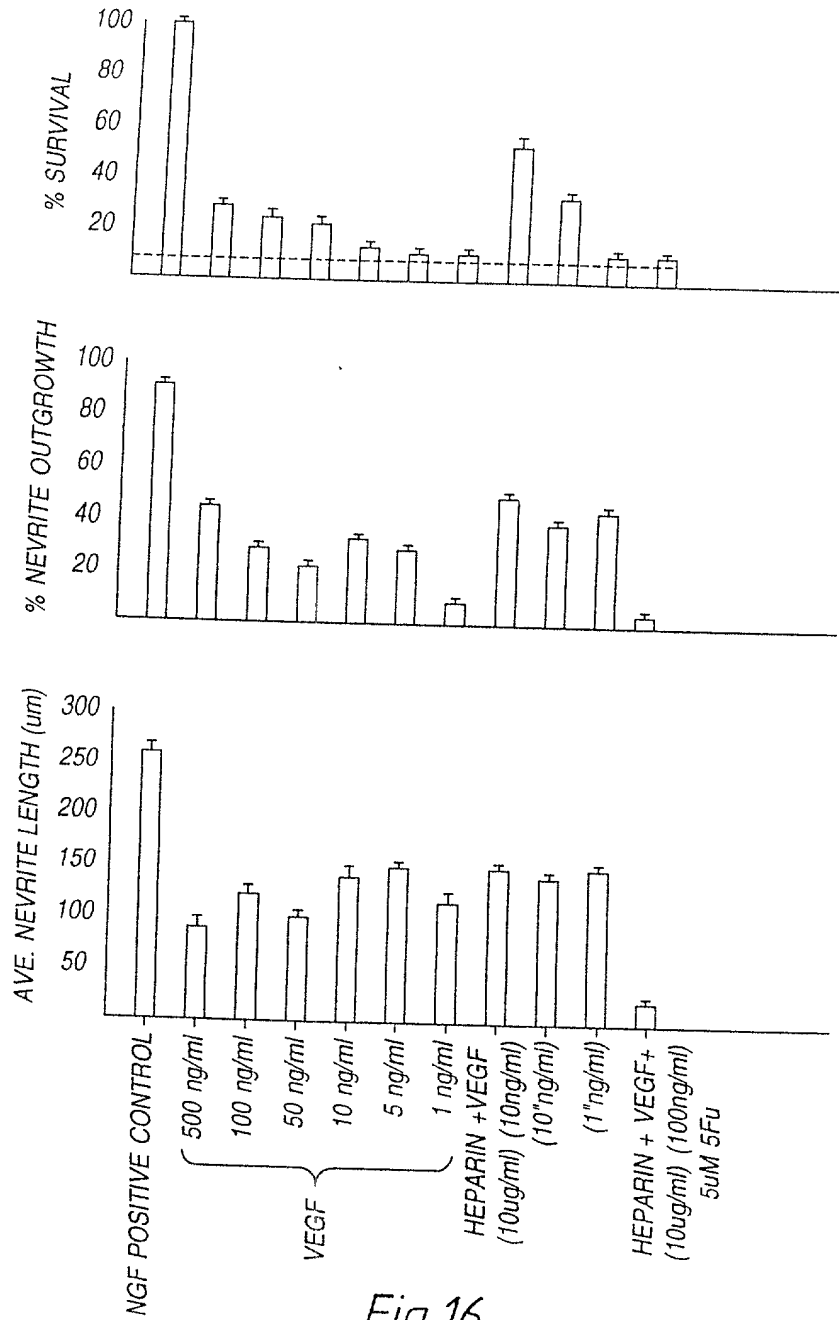


Fig. 16

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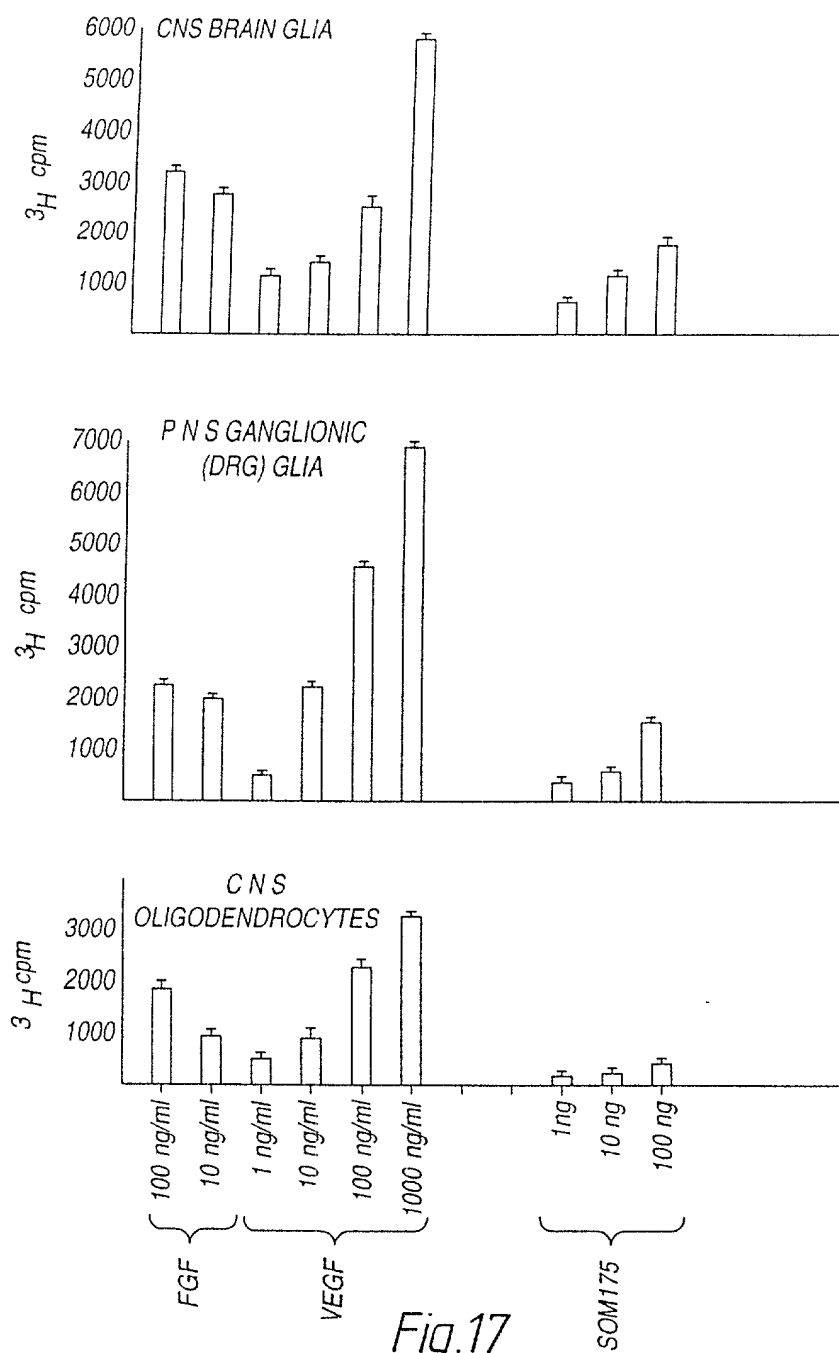


Fig.17

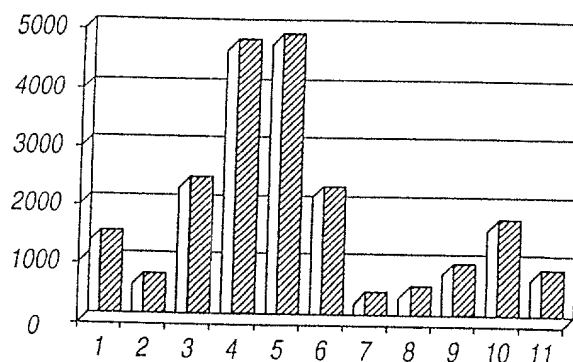


Fig.18

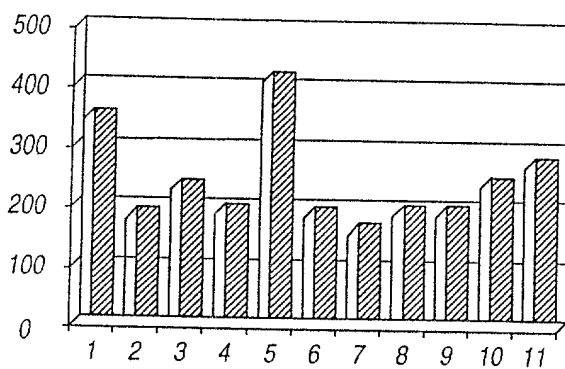
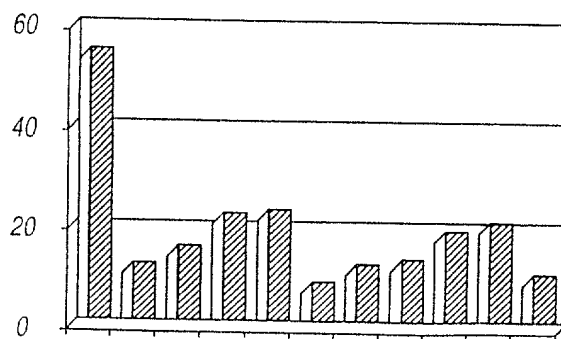


Fig.19



Fin 20